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EXAMINER	
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1634	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,956	SMITH ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 1992* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *6-12 and 14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,13 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *14* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-5 in Paper No. 13 with traverse is acknowledged. Applicant's further election of the single polymorphism at position 245 of EMBL ACCESSION NO. X65181, with traverse in paper number 13 is also acknowledged. Further, Applicant's addition of claim 19 is acknowledged. Claim 19, which is encompassed within the elected method of claim 1, will be examined with the elected group.

2. In an interview on 24 September 2002 it was agreed that one additional method would be examined with the methods of diagnosis of a polymorphism (see paper number 14), since the methods of diagnosis of disease or treatment of disease are not distinct from the methods of diagnosis of polymorphisms, but are distinct from one another. Applicant elected to have methods of treatment of disease rejoined to the methods of diagnosis of a polymorphism in a telephone conversation on 10/17/02. Thus, claim 13 is rejoined to the elected group.

3. Applicant argues that the common property that joins each of the polymorphisms under section (f)(i)(A) of the administrative guidelines is that they are al alternatives of the same gene. However, by setting forth this argument, applicant is effectively arguing that each difference in the NK1R gene is joined to the other because they are differences. This is not persuasive. Applicant has not identified a common effect that is conferred on the NK1R gene by these polymorphisms nor any property that each version of the gene has in common. Applicant has not shown a common property that unifies these different forms of the NK1R gene with respect to one another. Thus, applicant has not bet the burden required by section (f)(i)(A).

4. Applicant further argues that the polymorphisms are all linked because they are nucleic acids. The examiner agrees. However, this feature cannot be considered a special technical feature that links each invention, because it is not a contribution over the prior art, as many hundreds of thousands of nucleic acids are known in the prior art.

5. Second, applicant argues that the inventions of claims 17-18 could readily be examined with that of claims 1-5. However, applicant's arguments do not address the fact that the claims do not share a special technical feature, as is required by the Unity of Invention procedures. The methods of claims 17-18 have separate goals and require separate steps than those of group 1.

6. Third, applicants point out that claim 1 covers a method of diagnosis involving determining the sequence at "one or more" of the nine specified positions that if the restriction requirement is allowed to stand it will limit applicants to claiming methods for determining the sequence at only one of the positions. This is not persuasive, nor is it necessarily accurate. Claims which particularly require the examination of more than one polymorphic site were not presented. The claims, as presented and restricted, only **required** the determination of the sequence at a single polymorphic site. The current claim set includes claim 19 which requires the examination of all nine listed polymorphic sites. This claim is not separated from the elected polymorphism, but this does not remove the fact that claims which require only one of the polymorphisms are still restricted one from another. The restriction requirement was based on the claim set as presented, not a hypothetical claim set. Thus, since the claims requires only the sequencing of a single position, and all thirteen of the recited positions are independent and distinct from one another and the search and examination of all three separately would pose a

significant burden to the examiner, the requirement that applicant select a single polymorphism for examination is proper. The requirement is therefore made FINAL.

Specification

7. The disclosure is objected to because of the following informalities: The specification and claims repeatedly refer to EMBL accession numbers instead of reciting sequences or sequence identifiers. This recitation is similar to the recitation of a trademark, in that the EMBL accession number does not represent a fixed disclosure of a sequence, but instead refers to a record that is constantly able to be updated and modified. Applicant should amend the specification to include the sequences which are referred to by EMBL accession numbers (and comply with the remainder of the sequence rules) and file a 132 declaration with evidence showing and stating that the newly filed sequence is identical to the sequence that was in EMBL at the time the invention was filed.

8. The specification is objected to because there is no description of the drawings.

9. The specification is objected to because it do not comply with the sequence rules. Namely, the specification recites nucleic acid sequences which are not properly labeled with sequence identifiers (see at lease page 25 of the specification). See 37 CFR 1.821 through 1.825.

Claim Objections

10. Claim 4 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits individually. Where a rejection applies to all of the claims that claim 4 depends from, claim 4 has been included in the interest of compact prosecution.

11. Claim 19 is objected to because it recites polymorphisms at positions 461 and 495 of EMBL ACCESSION NO. 461 and 495 twice.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1, 2, 3, 4, 5, 13, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 13 are is indefinite over the recitation "determining the sequence of the nucleic acid of the human at one or more of positions..." because it is unclear how you determine a sequence at a single position of a nucleic acid. The word "sequence" implies the determination of the nucleotide present at more than one position of a nucleic acid, yet the claims set forth that the sequence is determined at one or more of the recited positions. It is not clear how a sequence can be determined at a particular position. Amendment of the claim to recite, for example, "determination of the nucleotide present at position 245 of EMBL ACCESSION NO. X65181" would obviate this rejection. Claims 2, 3, 4, 5, and 19 are also indefinite for this reason because they depend from claim 1 but do not clarify the issue.

Claims 1-5, 13, and 19 are indefinite over the recitation of EMBL accession numbers (X63179 and X65181) because it is not clear as to what is encompassed by this phrase. The sequences listed in the EMBL database are continuously updated and modified. Therefore, there

is no single, fixed definition for the sequences presented as EMBL Accession No. X65181 and X65181.

Claims 1 and 13 are further indefinite over the recitation "determining the status of the human by reference to polymorphism" because it is not clear what this step is requiring. It is not clear what it means to determine the status of a human "by reference to polymorphism." Claims 2, 3, 4, 5, and 19 are also indefinite for this reason because they depend from claim 1 but do not clarify the issue.

In claim 3, the phrase "the potential polymorphism" lacks proper antecedent basis in the claims because the claims do not previously refer to a "potential" polymorphism.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-5, 13, and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting and sequencing the human neurokinin 1 receptor (NK1R) gene and portions thereof, does not reasonably provide enablement for methods which are limited to the detection of a polymorphism at position 245 of EMBL ACCESSION NO. X65181. Furthermore, the specification does not provide enablement for methods in which a polymorphism is diagnosed and then a NK1R ligand antagonist drug is administered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

This rejection applies to the instant claims insofar as they might be interpreted as methods for the detection of the presence or absence of particular single nucleotide polymorphisms. It applies to claim 13 insofar as the claim implies that there would be a connection between the step of detection of the polymorphism and the administration of the NK1R ligand antagonist drug. Insofar as the instant claims read generally on methods for sequencing the human neurokinin 1 receptor (NK1R) gene, this rejection does not apply. The teachings of the specification (at, e.g., pages 22-23) and of the prior art as exemplified by Takahashi et al. disclose methods of detecting and sequencing the NK1R gene and portions thereof. Such methods are encompassed by the instant claims as written, and a person skilled in the art could clearly practice methods of detecting and sequencing a known gene without further guidance. However, it is unpredictable as to whether one of skill in the art could use without undue experimentation methods requiring detection of the polymorphism at position 245 of EMBL ACCESSION NO. X65181 or methods for treatment which comprise detection of the polymorphism at position 245 of EMBL ACCESSION NO. X65181, which methods are also encompassed by the claims. Furthermore, it is unpredictable as to whether one of skill in the art could use without undue experimentation a method which requires the examination of thirteen different single nucleotide polymorphisms in the NK1R gene.

It is noted that the instant claims each recite methods which comprise the detection of nucleotide sequences at one or more of thirteen different polymorphic sites. A restriction requirement was set forth in which applicant was required to select a single polymorphic site for examination. Applicant selected the polymorphism at position 245 of EMBL ACCESSION NO. X65181. This enablement rejection considers only this site in the claims that recite

polymorphisms in the alternative. With regard to claim 19, many of the examples in this rejection are directed at the elected polymorphism, but it is to be understood that the rejection applies to claim 19 also which requires the examination of nine different polymorphic sites.

The instant claims are drawn to methods for the diagnosis of a polymorphism in an NK1R gene in a human. The methods comprise steps in which the particular nucleotide is detected at a particular position in different portions of the human NK1R gene. Claim 13 further comprises a step in which a NK1R ligand antagonist drug is administered in an "effective amount."

The specification teaches that asthma is a "NK1R ligand-mediated disease (see page 1)." Further, the specification provides nine polymorphisms in the NK1R gene. In particular, the specification teaches a polymorphic site at position 245 of EMBL ACCESSION NO. X65181, located exon 5 of the NK1R gene. The polymorphism is a deletion polymorphisms which results in a truncated form of the NK1R polypeptide when the gene is expressed. The truncation is the loss of C-terminal 26 amino acids (p. 25 of specification). The specification is silent with respect to the effect of this polymorphism on the biological activity of the NK1R gene, beyond the fact that it results in a truncated polypeptide. The specification does not discuss or demonstrate how this truncation effects the activity of the encoded polypeptide nor does the specification discuss or demonstrate the effect of any of the other eight recited polymorphisms on the biological activity of the gene. The specification does not disclose any relationship between the presence of this polymorphism a change in the activity or expression of the NK1R or between the presence of a particular allele of this polymorphism and any particular disease state or physiological condition.

The prior art provides does not provide any naturally occurring polymorphisms or mutations in the NK1R gene. Riitano et al. (Journal of Biological Chemistry Vol. 272, No. 12, pp. 7646-7655, 1997) studied the effects of genetically engineered mutations on the NK1R receptor and found that some changes in the amino acid sequence of the receptor alter the activity of the receptor (see Abstract, for example). The prior art does not teach any naturally occurring polymorphisms or mutations in the human NK1R gene. The prior art does not provide specific guidance with regard to the polymorphism identified herein as being at position 245 of EMBL ACCESSION NO. X65181, or any of the other polymorphism identified herein, whose examination is required by claim 19.

There is also a large body of knowledge in the prior art related to polymorphisms in general, and their association with diseases or disease states. The art is highly unpredictable with regard to the functionality of polymorphic sites in genomic DNA. After a screening assay identifies polymorphisms, it is unpredictable whether any such polymorphisms would be associated with any phenotypic trait, such as a disease state or a physiological state. For example, Hacker et al. were unable to confirm an association between a gene polymorphism and ulcerative colitis in a case where prior studies suggested such a relationship would exist since the relationship had been identified in a different population (Gut, 1997, Vol. 40, pages 623-627). Even in cases where an association between a particular gene and a disease state is known to exist, such as with the LPL gene and heart disease risk or the β-globin gene and sickle cell anemia, researchers have found that when using SNP (single nucleotide polymorphism analysis) it was difficult to associate SNPs with disease states or to even identify key genes as being associated with disease (Pennisi, Science, 281 (5384):1787-1789). Finally, in some cases where

multiple polymorphisms are identified in a gene, some of these are demonstrated to be disease associated and some are not. Blumenfeld et al. (WO 99/52942) disclose a number of polymorphisms in the FLAP gene. While Blumenfeld et al. were able to demonstrate that some of these polymorphisms are associated with patients having asthma but some of these are not (see Figure 3). For example, the marker 10-35/390 was demonstrated to be associated with asthma, with a p value of 0.00229, while the marker 10-33/327 was determined to not have a statistical association with asthma (p=0.294). Thus, even for SNPs within the same gene, it is highly unpredictable as to whether a particular marker will be disease associated.

The level of skill in the pertinent art is quite high, i.e. generally a PhD in biochemistry, but the unpredictability in the art is higher. While the instant specification has disclosed a number of different polymorphisms in the NK1R gene, it remains highly unpredictable as to the biological significance of these polymorphisms. While the specification teaches that the elected polymorphism results in a truncation of the NK1R gene, the specification is silent as to how this truncation effects the functioning of the encoded polypeptide. Thus, the claimed method directed towards the diagnosis of polymorphisms, or treatment of disease following diagnosis of polymorphisms, for enablement of the full scope, requires the knowledge of unpredictable and potentially non-existent associations between the instantly elected polymorphism and some phenotypic trait. Even if the elected polymorphism is in some way associated with some disease, it is difficult (if not impossible) to know or predict from the teachings of the specification which disease or how the polymorphism is associated. That is, it is unpredictable as to whether the presence of a particular allele the polymorphism would confer a higher or lower likelihood of having the disease. In this case, the possible uses for the claimed methods are undefined, beyond

the suggestion that they can be used to detect a disease associated with the NK1R gene prior to treatment with a NK1R drug.

The amount of direction or guidance presented in the specification with regard to how to use the instant invention is minimal. With regard to claims directed towards simple detecting the presence of the gene polymorphism, applicant speculates that "differences in protein regulation arising as a result of allelic variation may have a direct effect on the response to an individual to drug therapy (p. 10-11)," but the specification does not elucidate the particular effects of any of the instantly disclosed polymorphisms on a response to drug therapy. Further, with respect to the elected polymorphism, the specification teaches that "Testing for the presence of this polymorphism is especially preferred because, without wishing to be bound by theoretical considerations, of its association with a signification loss of amino acids (p. 5)." Since the effects of any given polymorphism on gene activity are highly unpredictable, it is impossible to predict from the teachings of the instant specification what identifications can be made using the instantly claimed methods. That is, the specification does not provide any guidance as to how the polymorphism at position 245 of EMBL ACCESSION NO. X65181 would be associated with any pharmaceutical agent. The specification does not discuss whether this particular polymorphism will increase the likelihood of a positive or negative response to any drug. Furthermore, with regard to claim 13, which recites a method of treatment of a NK1R disease, the specification does not provide any guidance as to what disease is in fact associated with the presence or absence of the polymorphism at position 245 of EMBL ACCESSION NO. X65181, other than the suggestion that these methods could be carried out for "NK1R mediated diseases." The specification further fails to provide any guidance as to the appropriated NK1R drug to be

administered after the detection of the polymorphism, or the desired effect of administration of the drug (i.e. to up or down regulate the activity of the gene, and how either of these is to be accomplished). The specification provides no guidance or working examples that teach or demonstrate the ability to use the disclosed polymorphic site as a marker for any disease in particular, or for disease in general, or how to use the disclosed polymorphism to select a proper course of treatment of a disease.

The quantity of experimentation required to discover how to use the instant invention is very high. In order to use the claimed invention, one would have to establish a relationship between the polymorphism at nucleotide 245 of EMBL ACCESSION NO. X65181 some physiological or disease state or some disease treatment method. Indeed, even to use the method of claim 1 to identify patients suited for particular pharmaceutical agents, one would need to know that the polymorphism at nucleotide 245 of EMBL ACCESSION NO. X65181 was in some way associated with response to some pharmaceutical agent. In order to obtain the type of information necessary to practice the claimed invention, one would be required to undertake the screening of hundreds or thousands of patients as well as possible hundreds of diseases or pharmaceutical agents. Even if such experiments were undertaken, it would still be unpredictable as to whether any associations would be detected, in light of the unpredictability of such associations, as already discussed. Thus, while one could perform further research to determine whether applicant's method would be useful in disease detection and/or treatment, it is unknown as to what the outcome of such research might be and as to whether any quantity of experimentation would result in the identification of an association between the deletion of a C polymorphism at position 245 and any disease or condition. Further, absent a teaching the C

deletion polymorphism at position 245 is not associated with such conditions, it is further unpredictable as to whether detection of the C deletion polymorphism at position 245 would be useful in predicting, e.g., the absence or decreased likelihood of such conditions.

Furthermore, it is noted that the practice of the invention of claim 13 requires the administration of a NK1R ligand antagonist drug. The specification provides examples of such drugs at pages 6-7. However, the specification does not disclose a relationship between treatment with these drugs and the polymorphism at position 245 of EMBL ACCESSION NO. X65181. The identification of a relationship between and the elected polymorphism would be highly unpredictable, requiring an extensive amount of research and experimentation.

Thus, in light of the nature of the invention, the state of the art, the high level of unpredictability in the art, the lack of direction or working examples in the specification, and the high quantity of experimentation that would be required to practice the claimed invention, it is concluded that undue experimentation would be required to use the instantly claimed invention. Thus, with respect to claims 1-5 and 19, although the specification certainly enables one to detect the presence of the polymorphism(s) (i.e. the "make" portion of 112 1st paragraph), it would require undue experimentation in order to determine how to use the methods of claims 1-5 and 19. It would also require undue experimentation to make and use the method of claim 13. Considering all of the factors discussed herein, it is concluded that it would require undue experimentation to determine the particular disease state that can be diagnosed and treated and thus to practice the claimed invention commensurate in scope with the present claims.

Claim Rejections - 35 USC § 101

16. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

17. Claims 4, 5, and 13 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

It is noted that the instant claims each recite methods which comprise the detection of nucleotide sequences at one or more of thirteen different polymorphic sites. A restriction requirement was set forth in which applicant was required to select a single polymorphic site for examination. Applicant selected the polymorphism at position 245 of EMBL ACCESSION NO. X65181. This utility rejection considers only this site in claims 4, 5, and 12.

The instant claims are drawn to methods for the diagnosis of a polymorphism in an NK1R gene in a human and methods for treatment of disease in which the polymorphism is identified and then a drug is provided. Each of the methods comprise steps in which the particular nucleotide present is detected at a particular position in EMBL ACCESSION NO. X65181.

The specification teaches that the NK1R gene has been associated with a number of diseases and physiological states. Further, the specification provides thirteen polymorphisms in the NK1R gene. In particular, the specification teaches a polymorphic site at position 245 of EMBL ACCESSION NO. X65181. The specification teaches that the disclosed polymorphism in the exon 5 region of the NK1R gene results in a premature termination codon and the loss of 26 amino acids from the C-terminal portion of the encoded polypeptide. The specification teaches that polymorphisms in the NK1R gene may be associated with drug response.

Furthermore, the specification suggests that the methods can be used to detect a NK1R mediated disease.

None of these asserted utilities meet the standard of being specific, substantial, and credible. Generally, these are utilities that can be assigned to a broad class of invention, that is any method for detecting a polymorphism, thus they are not specific. Furthermore, the utilities set forth are not considered to be substantial because further experimentation would be required to reasonable confirm that the disclosed polymorphism is in fact diagnostic or prognostic of disease or in fact associated with the suitability of a particular pharmaceutical agent. The specification merely postulates that such utilities exist, but in order to practice the claimed invention, further experimentation would be required to determine an association between the polymorphism and some physiological state or disease.

Claims 4, 5 and 12 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The utility rejection has not been applied to claims 1-3 and 19 because these claims encompass an embodiment that would have utility, namely the sequencing of the NK1R gene, which itself is known to be associated with physiological and disease states. If the claims are narrowed to exclude this embodiment, these claims may be included in the utility rejection.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 1, 2, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Takahashi et al. (Eur. J. Biochem, 204, 1025-1033 (1992)).

Takahashi et al. teach a method for the diagnosis of a polymorphism in an NK1R gene in a human which comprises determining the sequence of the nucleic acid of the human at position 245 of EMBL ACCESSION NO. X65181, and determining the status of the human by reference to polymorphism in the NK1R gene (p. 1027 and FIG. 2). Furthermore, Takahashi et al. teach a method wherein the sequence is determined at all nine of the nucleotide positions recited in claim 19. Specifically, Takahashi et al. teach a method for sequencing the NK1R gene (p. 1027). The sequence provided by Takahashi et al. includes each of the polymorphic sites recited in the claims. This reference is considered to teach the invention of claims 1, 2, and 19 because the method contains only two method steps, one in which the sequence at the particularlly recited positions of the NK1R gene is determined (i.e. which is inherently accomplished by sequencing the portion of the gene that overlaps with position 245 of EMBL ACCESSION NO. X65181, for example), and one in which the "status of the human by reference to polymorphism" is determined. Determining the sequence of the gene is considered to inherently determine the status of the human by reference to the polymorphism because by sequencing the nucleotide present at position 245, the status of the polymorphism is determined.

Conclusion

20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C Einsmann
Examiner
Art Unit 163434

November 18, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600